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ORIGINAL ARTICLE

Probiotic mixture of *Lactobacillus helveticus R0052* and *Bifidobacterium longum R0175* attenuates hippocampal apoptosis induced by lipopolysaccharide in rats

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Abstract
In recent years, the beneficial impact of targeted gut microbiota manipulation in various neurological disorders has become more evident. Therefore, probiotics have been considered as a promising approach to modulate brain gene expression and neuronal pathways even in some neurodegenerative diseases. The purpose of this study was to determine the effect of probiotic biotherapy with combination of *Lactobacillus helveticus R0052* and *Bifidobacterium longum R0175* on the expression levels of proteins critical to neuronal apoptosis in hippocampus of lipopolysaccharide (LPS)-exposed rats. Four groups of animals (Control, LPS, Probiotic + LPS, and Probiotic) were treated with maltodextrin (placebo) or probiotic (10^9 CFU/ml/rat) for 2 weeks by gavage. On the 15th day, a single intraperitoneal dose of saline or LPS (1 mg/kg) was injected and 4 h later, protein assessment was performed by western blotting in hippocampal tissues. LPS significantly increased the Bax, Bax/Bcl-2 ratio, and cleaved caspase-3 expression along with decreased the Bcl-2 and procaspase-3 protein levels. However, probiotic pretreatment (*L. helveticus R0052* + *B. longum R0175*) significantly downregulated the Bax and Bax/Bcl-2 ratio accompanied with upregulated Bcl-2 expression. Prophylactic treatment with these bacteria also attenuated LPS-induced caspase-3 activation by remarkably increasing the expression of procaspase-3 while reducing the level of cleaved caspase-3 in target tissues. Our data indicate that probiotic formulation (*L. helveticus R0052* + *B. longum R0175*) alleviated hippocampal apoptosis induced by LPS in rats via the gut-brain axis and suggest that this probiotic could play a beneficial role in some neurodegenerative conditions.

Keywords Gut microbiota manipulation · Probiotic · Apoptosis · Lipopolysaccharide · Neurodegenerative disease · Gut-brain axis

Introduction

The gut microbiota represents the largest repository of microbes containing nearly 10^{13}–10^{14} microorganisms from over than 1000 species dominated by bacteria in human gastrointestinal (GI) tract (Gill et al. 2006; Qin et al. 2010). There is an emerging evidence for the bidirectional connection between the gut microbiota and the central nervous system (CNS), known as the gut-brain axis (Cryan and Dinan 2012; Bauer et al. 2016). Indeed, alterations in the composition of the intestinal microbiota can play a critical role in the pathogenesis of several neurological diseases (Marizzoni et al. 2017; Sherwin et al. 2017; Kim et al. 2018). In this regard, the use of probiotics (i.e., live microorganisms) is an interesting and

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